

Amendments to the Specification

Please replace the paragraph beginning on page 21, line 22 with the following paragraph:

FIGURES 1A and 1B ~~FIGURE 1~~ show ~~shows~~ nucleotide (A) and corresponding amino acid (~~B~~) sequence of the LAP-mIFN β construct. The boxed sequence corresponds to the sequence of the MMP cleavage site including linker sequence;

Please replace the paragraph beginning on page 22, line 1 with the following paragraph:

FIGURES 2A and 2B ~~FIGURE 2~~ show ~~shows~~ nucleotide (A) and corresponding amino acid (~~B~~) sequence of the mIFN β -LAP construct. The boxed sequence corresponds to the sequence of the MMP cleavage site including linker sequence;

Please replace the paragraph beginning on page 22, line 4 with the following paragraph:

FIGURES 3A and 3B ~~FIGURE 3~~ show ~~shows~~ amino acid sequences of the precursor domain of TGF β 1, 2, and 3 (human, Hu), TGF β 4 (chicken, Ck), TGF β (frog, Fg). Arrows indicate the position of the proteolytic processing resulting in cleavage of the signal peptide of TGF β 1 and of the mature TGF β s. N-linked glycosylation sites are underlined, as is the integrin cellular recognition sequence (Roberts and Sporn, Peptide Growth Factors and their Receptors: Sporn, MB and Roberts, AB, Springer-Verlag, Chapter 8, 422 (1996));

Please replace the paragraph beginning on page 22, line 12 with the following paragraph:

FIGURES 4A-4D ~~FIGURE 4~~ show ~~shows~~ the sequences of protein cleavage sites of matrix metalloproteinases (MMPs) (Nagase and Fields, Biopolymers, 40, 399-416 (1996));

Please replace the paragraph beginning on page 22, line 15 with the following paragraph:

FIGURES 5A and 5B ~~FIGURE 5~~ show ~~shows~~ schematic representation of the fusion proteins used in this study and their putative folding. (A) Primary structure of recombinant latent protiens. The linear

sequence arrangement of the LAP, MMP and mIFN β constituents in the two configurations used in this study, LAP-mIFN β and mIFN β -LAP, is shown. The box at the amino terminal end of LAP-mIFN β and mIFN β -LAP depicts the native signal sequence peptide for secretion of either TGF β or mIFN β respectively. (B) Putative folding and interactions with LTBP of latent cytokine. In LTBP, the EGF like repeats are shown as small squares, the cysteine-rich repeats and hybrid domain as circles, and the 'hinge region' which is sensitive to proteolytic cleavage is shown as a solid black line. Disulphide bonds are shown as solid grey lines; nucleotide (A) and corresponding amino acid (B) sequence of the LAP-mIFN β construct. The boxed sequence corresponds to the sequence of the MMP cleavage site including linker sequence;

Please replace the paragraph beginning on page 23, line 16 with the following paragraph:

FIGURES 8A-8B ~~FIGURE 8~~ show ~~shows~~ immunoprecipitation of MTX-selected CHO cell supernatants with anti-LAP and anti-IFN β antibodies and cleavage with MMP1, MMP3 and synovial fluid from rheumatoid arthritis patients. (A). LAP-mIFN β and (B). mIFN β -LAP. Untreated supernatants (lanes 1 and 5), MMP1 treated (lanes 2 and 6), MMP3 treated (lanes 3 and 7) and rheumatoid arthritis synovial fluid treated (lanes 4 and 8). Immunoprecipitated with anti-LAP (lanes 1-4) and anti-

IFN β monoclonal antibody (lanes 5-8). The positions of LTBP and fusion proteins are indicated by arrows. The arrows marked with an asterisk (*) indicate ~~indicates~~ the presence of MMP cleavage products;

Please replace the paragraph beginning on page 23, line 26 with the following paragraph:

FIGURES 9A and 9B ~~FIGURE 9~~ show ~~shows~~ kinetics of IFN activity following incubation in medium alone or with rheumatoid arthritis synovial fluid. (A). ~~A.~~ LAP-mIFN β ; (B). ~~Panel B.~~ mIFN β -LAP.

Please replace the paragraph beginning on page 24, line 1 with the following paragraph:

FIGURES 10A and 10B ~~FIGURE 10~~ show ~~shows~~ the inhibition of collagen-induced arthritis by DNA injection with LAP-IFN β . Panel A shows hind paw swelling and Panel B shows clinical score development from time of boost with collagen type II.

Please replace the drawings at the end of the specification with the formal replacement drawings filed herewith.